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**Participant Information Sheet**

Study Doctor: Dr Rohini Sharma

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**1. Invitation Paragraph**

You are being invited to take part in this research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

**2. Study Title**

**LANTana: Lutathera and ASTX727 in Neuroendocrine Tumours**

**The epigenetic modification of somatostatin receptor-2 to improve therapeutic outcome with Lutathera in patients with metastatic neuroendocrine tumours**

**3. What is the purpose of the study?**

The purpose of this study is to test how well pre-treatment with a drug called ASTX727 works in participants with neuroendocrine tumours that have spread to other parts of the body. ASTX727 is a combination of two drugs; cedazuridine and decitabine. Cedazuridine increases the amount of decitabine that enters the bloodstream, while decitabine is a type of drug which helps stop cancer cells from reproducing.

In this study, ASTX727 will be used to treat participants with metastatic neuroendocrine tumours (NETs) to see what effect it has on the subsequent therapy given – Lutathera which is a type of radioactive targeted therapy that delivers strong radiation directly into tumor cells and works by causing death of the cancerous tissues in NETs. The actions of Lutathera and ASTX727 will be described more in Section 9. Lutathera has already been approved for use in the UK against NETs, however ASTX727 is still being tested in clinical trials such as this one. The ASTX727 clinical program includes a total of 7 clinical trials, including 309 patients. One clinical trial included 8 healthy volunteers and the rest of the ongoing studies involve patients with myelodysplastic syndromes (MDS) which are a group of disorders caused by blood cells that are poorly formed or don't work properly and with chronic myelomonocytic leukaemia (CMML) which is a rare type of blood cancer.

**4. Why have I been chosen?**

You have been invited because you have neuroendocrine tumours and on PET imaging you have expressed low or no uptake of the tracer used in the scan. Participation in the study is an option and may not be the only form of treatment you can have.

About 27 participants with metastatic NETs in the UK are expected to participate in the study. The duration of your participation is expected to be up to a year. After 2 months from completing all study treatments, or after you are withdrawn from treatment, you will be asked to attend a follow-up visit to monitor for possible side effects and potential benefits. The follow-up visits will continue 3-monthy thereafter.

**5. Do I have to take part?**

No, it is up to you to decide whether or not to join the study. Even if you do decide to take part, you are free to withdraw at any time, without giving a reason. This would not affect your future medical care in any way.

If you agree to take part, you will be given this information sheet to keep and be asked to sign a consent form.

**6. What will happen to me if I take part?**

You will be assigned to receive 5 days worth of ASTX727 every 56 days with a daily dose of 100mg cedazuridine and 35mg decitabine. Lutathera will then be administered on Day 8 of every cycle from Cycle 2. It will be given by intravenous (IV) infusion, which involves inserting a needle attached to a cannula (like a small straw) into a vein in your hand. The infusion will take around 30 minutes each time and a pump will be used to ensure that the medicine is given over the proper amount of time.

ASTX727 is an oral drug and will be dispensed as red, oval-shaped film coated tablets. You will be asked to take one tablet a day for 5 consecutive days at the start of each cycle.

This is an ‘open label’ study, which means that you and your physician will know what drugs you will be given.

There are three periods to the study: screening, treatment and follow-up. All study visits will be at a hospital within the NHS trust where your study doctor works. A summary of the schedule of visits and procedures/assessments is provided on Section 8. Each visit may take a few hours to complete, so you should set aside a whole day for each one. The study team will do their best to minimise waiting times and make you comfortable during visits, including providing food and drink during the longer ones.

**Screening**

Certain examinations and tests, which we may refer to as screening tests, are required to help your study doctor determine whether you are eligible for this study. The screening period of the study can take between 1 to 28 days to complete and may include more than one study visit in order to complete the various procedures.

Before any study-related procedures that are not standard of care are performed, you will be asked to read this information and sign the attached consent forms. It is your right as a participant to have the study fully explained to you and you can ask your study doctor to explain or go over any parts of this information, or the consent form, that you do not understand.

The following tests and procedures will be performed by the study staff to determine whether you are eligible to participate in this study:

* Review of your medical history; you must not have known HIV infection
* Review of medications you are currently taking and have taken in the past, including herbal medications
* A physical examination including measurement of your height, weight and vital signs
* (temperature, blood pressure, respirations and heart rate)
* You will be asked about the symptoms you are having from your disease (performance status)
* Collection of your blood (approximately 6 teaspoons/30 mL) for laboratory tests to check your general health, for hepatitis B or C infection and pregnancy (women only), and for monitoring your disease
* Optional collection of blood (approximately 11 teaspoons/55 mL) for further study of your disease
* Biopsy of tumour tissue. Furthermore, if you have had a tumour biopsy or cancer surgery in the past, samples will be requested from the medical facility where it was done. In order to participate in this study, you must give us your consent to obtain these original samples and allow your study doctor to send them to an external laboratory for tests to study your disease.
* Tumour assessments consist of CT Scans: computed tomography scan is a medical imaging technique used in radiology to get detailed images of the body noninvasively

Positron emission tomography (PET) scan - an imaging procedure which uses a radioactive drug referred to as a tracer to show how well your tissues and organs are functioning.

* You will be asked to complete Quality of Life questionnaires to assess how you are tolerating the treatment and to find out how well you are doing

If, based on the results of the screening visit tests and procedures, you are eligible to participate in the study, you will return to the hospital for treatment.

It is possible that after the results are reviewed you may not be eligible to take part in this study. Or, even though you may meet all the criteria for participation, your study doctor may decide not to enrol you in this study. In either of these situations, your study doctor will discuss other treatment options with you.

**Treatment**

The treatment period will consist of four 56 day cycles except 1 28 day cycle which is cycle 1. You will be given ASTX727 on Day 1 of each cycle and you must fast for a total of 4 hours on those days. Fasting (no food, milk or alcohol) begins 2 hours pre-dose and continues through 2 hours post-dose.

Lutathera will be administered by IV infusion.

Every time you come in to pick up your prescription for ASTX727 the following assessments will be performed:

* Review of your symptoms and medications
* A physical examination as required by your symptoms, and measurement of your weight and vital signs. Your vital signs will also be taken the first time you have Lutathera.
* Collection of your blood (approximately 5 teaspoons/25 mL) for laboratory tests to check your general health and hepatitis viral load (if required), and to monitor your disease
* A GFR (Glomerular Filtration Rate) prior to the first cycle is required which is a type of scan which occurs after the PET scan to check how well your kidneys work which will involve the injection of a very small amount of radioactive tracer and subsequent blood sampling . Collection of urine for laboratory tests to check your general health

On Day 8 of Cycle 2 - 5, Lutathera will be administered by an IV infusion. If you experience any changes in your body or develop any new or worsening symptoms during or after a study drug infusion you should inform the study doctor or nurse immediately. Because Lutathera is a radioactive treatment, you will be asked to take some precautions following therapy to minimise the radiation dose to your friends and family. We will discuss this with you in more detail when you attend for treatment. Including the standard SPECT/CT scans after your therapy to check whether this has been successful.

You will have 6 CT-scans which are part of your routine care. If you take part in this study you will not undergo any additional scans. These procedures use ionising radiation to form images of your body and/or provide treatment and/or provide your doctor with other clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The chances of this happening to you are the same whether you take part in this study or not.

You will also have a PET scan, on Day 8.

On both days of your visit at screening and cycle 1 Day 8 we will inject the radiotracer into a vein in your arm or hand about an hour before your scan, as it takes time for it to reach the right cells in your body. It's important to relax, keep as still as possible, and avoid talking while you wait because moving and speaking can affect where the radiotracer goes in your body. During the scan, you lie on a flat bed that's moved into a large cylindrical scanner while the scanner takes pictures of your body. These pictures will allow your doctor to monitor whether the drug ASTX727 is having the desired effect on your disease.

The scan usually takes 30 to 60 minutes. Having the scan is completely painless, but you may feel uncomfortable lying still for this long. You shouldn't experience any side effects after having a PET scan and can usually go home the same day

You may be discontinued from treatment based on your disease assessments, or because of possible side effects of the study therapy. Based on discussion between you and your study doctor, you may discontinue for other reasons.

**Follow-up**

After finishing the treatments, you will be asked to continue to come in for a follow-up visit every 3 months until the disease worsens or you decide you no longer wish to be part of the trial and the following procedures and assessments will be performed:

* A physical examination as required by your symptoms, and measurement of your vital signs.
* Collection of your blood (approximately 5 teaspoons/25 mL) for laboratory tests to check your general health and to monitor your disease.

You will also be asked to complete Quality of Life questionnaires at these visits.

**7. Will my costs be covered?**

You will be reimbursed for reasonable travel expenses related to your participation in the study on the relevant visits. This is not applicable to visits which would have occurred regardless whether you are on this study

**8. What will I have to do?**

You will need to attend all scheduled study visits as described in Section 6 and summarised in the table below.

Apart from the study drugs we administer to you it is important that you take any other prescribed medications as directed.

You must inform your study doctor of any non-study medication or therapy that you have from Screening until the first Follow-up Visit.

You must not enter any other research studies nor be participating in other clinical trial using investigational products whilst participating in this study.

You will be given a subject alert card (providing the contact details of your study doctor) to remind you and others that you are in a research study. Please carry this card with you at all times, if you need to seek emergency care, or if hospitalisation is required, please inform the treating doctor that you are participating in a research study.

The requirements for contraception and reporting pregnancy, are described in detail in Section 13.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Time point →**  **Assessment ↓** | **Screening** | **Cycle 1** | | **Cycle 2** | | **Cycle 3** | | **Cycle 4** | | **Cycle 5** | | **3 monthly follow up** |
|  | **Day -28 to -1** | Day 0 | Day 8 +2 | Day 0 | Day 8 +2 | Day 0 | Day 8 +2 | ,Day 0 | Day 8 +2 | Day 0 | Day 8 +2 |  |
| Informed Consent | X |  |  |  |  |  |  |  |  |  |  |  |
| Medical History | X |  |  |  |  |  |  |  |  |  |  |  |
| Demographics | X |  |  |  |  |  |  |  |  |  |  |  |
| Height | X |  |  |  |  |  |  |  |  |  |  |  |
| Vital Signs | X |  | X | X | X | X |  | X |  | X |  | X |
| Physical Exam | X |  | X | X |  | X |  | X |  |  |  | X |
| ECOG Performance Status | X |  | X | X |  | X |  | X |  | X |  | X |
| Pregnancy Test | X | X |  | X |  | X |  | X |  | X |  |  |
| Haematology | X |  | X | X |  | X |  | X |  | X |  | X |
| Biochemistry | X |  | X | X |  | X |  | X |  | X |  | X |
| [68Ga]-DOTA-TATE | X |  | X |  |  |  |  |  |  |  |  |  |
| GFR Measurement | X |  |  |  |  |  |  |  |  |  |  |  |
| Tumour Assessments (mRECIST) \* | X |  |  |  |  |  |  | X |  |  |  | X |
| SPECT/CT scan |  |  |  |  | X |  | X |  | X |  | X |  |
| Archival Tissue | X |  |  |  |  |  |  |  |  |  |  |  |
| Fresh Frozen Research Biopsy – Mandatory |  |  | X |  |  |  |  |  |  |  |  |  |
| Research Bloods |  |  | X | X | X | X |  |  | X |  | X |  |
| Quality of life questionnaires | X |  |  | X |  | X |  | X |  | X |  | X |
| Lutathera administration |  |  |  |  | X |  | X |  | X |  | X |  |
| ASTX727 administration |  | X |  | X |  | X |  | X |  |  |  |  |
| Adverse Events |  | X | X | X | X | X | X | X | X | X | X | X |

\* CT Scans

**9. What is the drug or intervention that is being tested?**

ASTX727 as mentioned above is a combination of two active drugs; cedazuridine and decitabine. Cedazuridine is a novel product and is a cytidine deaminase (CDA) inhibitor whereas decitabine is a regulatory approved drug but for IV infusion. Cedazuridine prevents the breakdown of decitabine by binding to CDA and blocking it from carrying out its usual function as primarily a gut and liver enzyme that degrades specific protein structures. This increases the availability of decitabine in the blood so it can carry out its own function which is to stop methyl groups from being added onto DNA and consequently also stimulate expression of the protein SSTR2 (somatostatin receptor 2) on neuroendocrine tumour cells. Although, decitabine on its own is actually an approved therapy for a type of cancer; acute myeloid leukaemia (a cancer of the white blood cells), this study is not assessing its effects as anti-cancer therapy but rather as an epigenetic modifier – how it changes the compounds in our bodies that tell our genes and DNA what to do and what proteins to make.

With more SSTR2 present on NETs, there are more cells for Lutathera to bind to. Lutathera,also called 177Lu-DOTA0-Tyr3-Octreotate, is composed of a somatostatin analogue or peptide that has been attached to a molecule which contains the radionuclide, lutetium-177. The radioactive lutetium delivers strong radiation directly into tumor cells and works by causing death of the cancerous tissues. The intent of giving the drug internally through an intravenous infusion is that it should focus the cell killing effects of the radiation by binding to tumors and because of the rapid excretion of the remainder have less effect on healthy tissue

**10. What are the alternatives for treatment?**

Other treatments available for your condition include:

* Getting treatment or care for your cancer without being in a study
* Taking part in another study of an investigational drug
* Getting no treatment

Talk to your doctor about your choices before you decide whether to take part in this study.

**11. What are the side effects of any treatment received when taking part?**

Treatments for cancer often have side effects, including some that are life-threatening. There is the possibility of death occurring as a result of this treatment regime and its side effects. There may be additional unknown risks.

If you experience severe side effects associated with the study drug, your doctor may prescribe medications to treat the side effect(s), future treatments may be delayed, or treatment may be stopped permanently. Any significant new findings that develop during the course of the research and may relate to your willingness to continue participation will be provided to you.

ASTX727 and Lutathera may cause the side effects listed below. The severity and duration of these side effects may vary for each participant. This information is based on data from participants in other clinical trials with these drugs. In addition, there may be side effects that are not yet known. **You should tell your study doctor or nurse about all symptoms you experience, whether or not you think they are caused by the study drugs.**

**ASTX727**

There are no known contraindications for cedazuridine; the only known contraindication for

decitabine is hypersensitivity. No warnings for cedazuridine have been identified at this time.

Warnings for decitabine include events related to myelosuppression (A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets) and foetal harm in pregnant women.

The AEs (Adverse Events) with the highest incidence (20% or more of subjects), regardless of relationship to ASTX727 included anaemia, thrombocytopenia (low blood platelet count), neutropenia (few neutrophils, a type of white blood cells), fatigue, constipation, nausea, diarrhoea, febrile neutropenia (neutropenia with fever), leukopenia (decrease in disease-fighting cells (leukocytes) in your blood), dizziness, decreased appetite, dyspnoea (experience of breathing discomfort), headache, cough.

SAEs (Serious Adverse Events) of the 385 subjects treated with cedazuridine plus oral decitabine (administered as separate capsules) or ASTX727 tablet, 247 subjects (64.2%) had SAEs which included febrile neutropenia (23.4%), pneumonia (13.5%), sepsis(7.3%), cellulitis (4.2%), anaemia (2.9%), pyrexia (2.9%) or high temperature and bacteraemia (the presence of viable bacteria in the circulating blood)

Women of childbearing potential and men with female partners of childbearing potential must use highly effective contraception and avoid pregnancy during participation in any studies of ASTX727.

**Lutathera**

Lutathera side effects are mainly linked to radioactivity. The most common radioactivity side-effects seen in participants being treated with Lutathera is the decrease of blood cells, most importantly, red blood cells, platelets (a special cell which helps the blood to clot), and other blood cells such as white blood cells (helps to fight infection). A decrease in the various blood cell types may put you at risk for bleeding, fatigue, shortness of breath and infection. This happens in many participants and is frequently temporary. If this does occur to you, we will let you rest for longer periods between treatments to allow the blood cells to return to normal levels. However if we see that your blood cells do not return to normal levels we will consider discontinuation from the clinical trial. Very rarely, Lutathera has been associated with Myelodysplastic Syndromes (MDS), a pre-stage of leukemia or blood cancer and leukemia.

The radioactive substance may affect other organs, especially kidneys, bone marrow, liver, spleen, and pituitary gland. In order to check the possible adverse effects of treatment with Lutathera on these organs, we will check the function of these organs before and during the study period by taking blood and urine tests.

Other side-effects of Lutathera include nausea and vomiting – usually during the first 24 hours and abdominal pain – during the treatment administration. Possible delayed (first 24 hours) side effects include fatigue and temporary hair loss. Additionally there is a possibility that due to an excessive release of hormones from the cancer following the administration of Lutathera, your doctor may request that you stay in hospital overnight for observation and treatment if necessary. Treatment, if required, normally consists of intravenous fluids (fluids directly given into a vein), to correct any chemical imbalance in the blood. If you have an increase of symptoms following treatment (such as diarrhoea, flushing, arrhythmia, shortness of breath), you must contact your doctor immediately. They will advise you on how to control your symptoms

Out of 944 subjects the most common side effects were 82 pancytopenia (a condition in which a person's body has too few red blood cells, white blood cells, and platelets), 32 anaemia and 21 Thrombocytopenia (low blood platelet count**)**. 14 showed MDS and 9 abdominal pain. Uncommon Nausea 8 and vomiting and/or Leukopenia 7.

Rare side effects (less than 4) include diarrhoea, constipation, lymphopenia (reduced level of a certain type of blood cell called a lymphocyte), Malaise (general feeling of discomfort, illness or unease whose exact cause is difficult to identify), Acute renal injury, Renal failure, Acute myeloid leukaemia (type of blood cancer), Tumour lysis syndrome (metabolic abnormalities), Weight decreased, Fever, Bone marrow failure and very rare (less than 2) Cystitis, Pneumonia, Ascites (fluids that collect in your abdomen), Myocardial infarction, Carcinoid crisis, pain, Hyperbilirubinemia (or jaundice, too much bilirubin which causes yellow discoloration), decreased appetite, Hypercalcemia (calcium level above normal), dizziness, Hypotension (low blood pressure) and flushing (increase blood flow which causes sweating)

**Other side effects**

Side effects associated with blood tests or use of an IV catheter may include infection, bruising, redness, discomfort, or bleeding at the needle puncture site.

There may be risks or side effects which are unknown at this time.

Your condition may not get better or may become worse while you are in this study.

Certain drugs may increase the severity of these side effects if taken during the study. Ask your study doctor for a full list of prohibited medications.

**12. What are the other possible disadvantages and risks of taking part?**

To enrol in this study we are asking the first 5 participants to have a fresh tumour biopsy at Cycle 1 Day 8 in the treatment phase. Removal of tumour tissue would need to be done under local anaesthetic and can be painful and cause pressure or discomfort in the area where the tissue was taken. Pain and discomfort can last for several hours and up to several days after the biopsy procedure. You may experience redness, swelling, bruising or infection in the area where the tissue was taken, and/or feel faint or dizzy.

As part of your involvement in this study you will receive a number of PET scans of your body. PET scans use ionising radiation in the form of injected tracers. Exposure to ionising radiation carries with it a risk that it may cause cancer later in life, after a delay called the latency period. This latency period can be from 2-10 years for leukaemia, and up to several decades for solid tumours. The risk to a healthy 40-year old form the total radiation involved in this study is estimated to be about 1 in 129. For someone with your pre-existing condition, the chances of you taking part in this study and developing another cancer later on may be considered very small.

Occasionally during the course of a study you may be found to have a previously undiagnosed medical condition. In this situation your study doctor will take the necessary steps to ensure you receive appropriate treatment.

If you have private medical insurance, you may wish to check with the insurance company before agreeing to take part in the study, in case participation affects the validity of your insurance policy.

**13. Are there any risks for reproduction, unborn babies and breastfeeding infants?**

It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Women and men with female partners of childbearing potential must use highly effective contraception during the course of this study and for at least 6 months after the last dose.

*Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subjects*

Any woman who finds that she has become pregnant while taking part in the study should immediately tell her research doctor and you will be discontinued from the study. Additionally, you should not breastfeed your baby within 4 months following Lutathera treatment

Lutathera may cause infertility in males and females. The recommended cumulative dose may result in temporary or permanent infertility

ASTX727 (cedazuridine and decitabine) and Lutathera may have adverse effects on a foetus in utero. Furthermore, it is not known if ASTX727 has transient adverse effects on the composition of sperm. For this trial, male participants will be considered to be of non-reproductive potential if they have azoospermia (whether due to having had a vasectomy or due to an underlying medical condition).

In order to participate in the study you must adhere to the contraception requirement (described below) from the day of IMP administration (or 14 days prior to the initiation of study medication for oral contraception) for the duration of the study and for 6 months after the last dose of your Lutathera treatment.

• hormonal combined contraception containing estrogen and progestogen which stops the ovulation process, oral and injectable methods are by far the most popular.

• progestogen-only hormonal contraception which keeps the cervical mucus viscous so sperm cannot enter the uterus and fallopian tubes to fertilize an egg. Progestin also keeps the uterine lining in a condition that doesn't support implantation and nourishment of the fertilized egg •

• intrauterine hormone-releasing system (IUS) is a small, T-shaped plastic device that's put into your womb (uterus) by a doctor or nurse. It releases the hormone progestogen to stop you getting pregnant and lasts for 3 to 5 years, depending on the brand

• bilateral tubal occlusion or blocked fallopian tube. A nonsurgical form of permanent [birth control](https://www.medicinenet.com/birth_control_methods/article.htm) in which a physician inserts a 4-centimetre (1.6 inch) long metal coil into each one of a woman's two fallopian tubes. This allows tissue to grow over the coil to form a plug that prevents fertilized eggs from traveling from the ovaries to the uterus.

• vasectomised partner

• sexual abstinence

The relevant contraception methods acceptable for the participants as per the MHRA guidance <https://www.gov.uk/drug-safety-update/medicines-with-teratogenic-potential-what-is-effective-contraception-and-how-often-is-pregnancy-testing-needed>

**14. What are the possible benefits of taking part?**

There are limited treatment options for participants with advanced neuroendocrine tumours (NETs). It is the 11th most common cancer and the second most prevalent tumour of the gastrointestinal tract. Despite increasing prevalence, there has been no real change in prognosis over the last 20 years with advanced NETs mostly being incurable and resistant to most cytotoxic drugs. ASTX727 might increase the effects of Lutathera. The combination of ASTX727 and Lutathera might be better than routine treatments and might improve overall survival compared to other standard of care treatments.

However, treatment with ASTX727 and Lutathera might not lead to improvement of your cancer.

The knowledge gained from this study may also be of help to other participants with the same kind of cancer in the future.

**15. What if relevant new information becomes available?**

Sometimes during the course of a research study, new information becomes available about the treatment/drug that is being studied. If this happens, your study doctor will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your study doctor might consider it to be in your best interests to end your participation in this study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, you will be told why and your continuing care will be arranged.

**16. What happens when the research study stops?**

At the end of the study, the study drug will no longer be provided to participants. Your study doctor will ensure that you receive the appropriate standard care for your condition.

**17. What will happen if I do not want to carry on with the study?**

Your participation in this study is entirely voluntary. It is up to you to decide whether to take part or not. Even if you do decide to take part, you are free to discontinue treatment or withdraw consent from the study at any time without giving a reason. This will not affect your future medical care in any way.

Please note that any information collected before you withdraw will be kept and used to complete the research.

If you decide to stop study treatments, your study doctor will not presume that you have withdrawn from the study but will assume that you will continue to participate in any follow-up activities described in Section 6. If you do not want to participate in any or all follow-up activities, you must inform your study doctor in writing and clearly identify the activities you do not want do.

**18. What if something goes wrong?**

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator Dr Rohini Sharma on tel 02033133170. The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

You can also obtain independent advice from the Patient Advice and Liaison Service (PALS). PALS offers confidential advice, support and information on health-related matters, and can be contacted at the PALS office. Details can be obtained from the hospital.

**19. What will happen with my data, will my taking part in this study be kept confidential?**

Imperial College London, UK, is the sponsor for this study. It will be using information from you and your medical records in order to undertake this study*,* and will act as the data controller for this study. This means that it is responsible for looking after your information and using it properly. Imperial College London will normally keep personal data in relation to the consent forms and primary research data 10 years after the study has been completed.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

The NHS organisations hosting the study will collect information from you and your medical records for this research study in accordance with the instructions of Imperial College London. They will keep your name, NHS number and contact details confidential, and will not pass this information to Imperial College London. The NHS organisations will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Imperial College London and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Imperial College London will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

The NHS organisations will keep identifiable information about you from this study for at least 10 years after the study has finished.

Your coded study data may be shared by Imperial College London with its agents, collaborators and business partners, who may be located inside of the country or region in which you live, or outside (e.g. the USA, European Union). However, your study data will be kept confidential and secure.

Your study data may also be used in publications about this study but it will remain coded: your identity will not be revealed in any compilation, study report or publication at any time.

Your study doctor will ask for your permission to notify your GP about your involvement in this study. Your GP will be sent a letter about the study highlighting any important instructions related to your medical care while you are taking part in the study.

**20. What will happen to any tissue or other samples I give?**

Most blood and urine samples collected from you will be tested within the NHS organisation hosting the study, to check your health and monitor your disease.

Tumour tissue samples and optional blood samples, will be transferred to the research sponsor, Imperial College London. These samples will be labelled with a unique code instead of your name, and analysed in order to study your disease. Information derived from these samples will be handled by Imperial College London as described in Section 19 above.

At the end of the study, if there are any samples left over they may be transferred for indefinite, long-term storage in the Imperial College Healthcare Tissue Bank, which is licensed by the UK Human Tissue Authority. Your samples will be labelled with a unique code instead of your name or other details that could readily identify you. They may be used in future, ethically approved research to study liver cancer or other diseases. This future research may involve transfer of samples to Imperial College London's agents, collaborators and business partners who may be located outside of the country or region (e.g. the European Union) in which you live. However, your samples and data they provide will be kept confidential and secure.

If you withdraw from the study, any stored blood or tissue samples that can still be identified as yours will be destroyed if you wish. If you wish to withdraw your consent for such samples to be retained, you should let your study doctor know.

**21. Will any genetic tests be done?**

Yes. As part of this study, the sponsor would like to see if there is anything within your genes/proteins which may help them to understand or treat neuroendocrine cancer. This analysis will be completed on the sample of your tumour that was taken at the time of diagnosis, or during other surgical procedures, and on some of the blood samples that are taken from you. The future research mentioned in Section 20 might involve genetic tests also. You will not be contacted by the sponsor in connection with the research or given any information about the results of genetic tests performed on the samples that you provide for this research.

**22. What will happen with the results of the research study?**

The data collected will be used for the evaluation of the study, and may be used in the future in related or other studies. The data may be submitted in coded form to health authorities for registration purposes. Members of health authorities, such as the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK, Food and Drug Administration (FDA or other persons required by law may review the coded data provided. This data may also be used in publications about the study drug but the data will remain coded. Your identity will not be revealed in any compilation, study report or publication at any time.

**HOW WILL WE USE INFORMATION ABOUT YOU?**

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

* 10 years after the study has finished in relation to data subject consent forms.

We will need to use information from your medical records for this research project.

This information will include your

* initials
* NHS number
* name
* contact details

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

**LEGAL BASIS**

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publically-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research.  This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the [UK Policy Framework for Health and Social Care Research](https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/)

**INTERNATIONAL TRANSFERS**

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (**EC**) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

**SHARING YOUR INFORMATION WITH OTHERS**

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

* Other College employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.
* only anonymised data will be shared

**WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?**

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

* if follow up data will be collected after withdrawal
* We need to manage your records in specific ways for the research to be reliable. This means that we won’t be able to let you see or change the data we hold about you.

**WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED**

You can find out more about how we use your information

* at [www.hra.nhs.uk/information-about-participants/](https://www.hra.nhs.uk/information-about-patients/)
* by asking one of the research team
* by sending an email t*o study team* [*m.martinez@imperial.ac.uk*](mailto:m.martinez@imperial.ac.uk)
* by ringing us *on 020 33133170.*

**COMPLAINT**

If you wish to raise a complaint on how we have handled your personal data or wish to find out more about how Imperial College London will use your information at http://www.imperial.ac.uk/joint-research-compliance-office/research-governance/data-protection/ or by contacting the Data Protection Officer at dpo@imperial.ac.uk or on 020 7594 3502

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner’s Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

**23. Who is organising and funding the research?**

The academic institution organising ('sponsoring') this study is Imperial College London. The funding is from a pharmaceutical company, AAA – Advanced Accelerator Applications (A Novartis Company) who also provide Lutathera. Astex is providing the trial drug ASTX727.

The NHS organisations hosting the study will be paid for including you in this study.

**24. Who has reviewed the study?**

An NHS Ethics Committee, Leeds West Research Ethics Committee has reviewed the objectives and the proposed conduct of the study and has given a favourable opinion of it. The study has also been reviewed and authorised by the UK Medicines and Healthcare products Regulatory Agency, and approved by the UK Health Research Authority.

**25. Contact for Further Information**

If you have any questions regarding the study or in case of study related injury you should contact your study doctor – *Dr Rohini Sharma on tel 0203 3133170*

A description of this clinical trial will be publicly available on <https://clinicaltrials.gov>.

**Thank you for taking time to read this sheet.**

**You will receive a copy of this information sheet and the signed informed consent form should you wish to participate in this study.**